REMARKS

Applicants thank the Examiner for withdrawing the objections to the specification and some of the rejections under 35 U.S.C. §§ 101, 112 and 102 in view of Applicant's previous Amendment and Response. In this Amendment and Response After Final Rejection, Applicants further simplify the claims and bolster information presented in support of patentability of the claims. Claims 1, 2, 12 and 28 have been amended. Claim 29 has been canceled. Dependent claims 31-35 have been added. Support for new claim 35 can be found in the specification at, for example, paragraph [00142]. Claims 1-7, 12, 18, 25-28 and 30-35 are pending. The amendments will be discussed in regard to addressing the rejections and objections in the final office action in the paragraphs below.

Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The rejection of claim 1 and claims 3-7, 12, 18 and 25-26 dependent thereon under 35 U.S.C. §112, second paragraph was maintained as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner maintained the rejection of the term "simple sugar," whose definition he could not find in the cited paragraph [0042]. While not agreeing with the lack of a definition for this term, Applicants have deleted this term from claims 1, 12 and 28, thereby obviating this rejection. Applicants thus respectfully request that this rejection be withdrawn.

Rejection of Claims Under 35 U.S.C. §112, First Paragraph

The rejection of claim 1 and claims 2-7, 12, 18, 25-26 and 28-30 under 35 U.S.C. §112, first paragraph was maintained because allegedly the specification, while being enabling for a polynucleotide encoding a polypeptide with SEQ ID NO:2 and having a specific glycosyltransferase activity, vectors and host cells comprising said polynucleotide and a method of making said polypeptide using the host cell comprising said polynucleotide, does not reasonably provide enablement for any such polynucleotide that is at least 95% identical to SEQ ID NO:1 or 3 or any polynucleotide which encodes a polypeptide comprising an amino acid sequence of at least 90% or 95% identity to SEQ ID NO:2, or a polypeptide comprising 285 contiguous amino acids of or comprising a glycosyltransferase domain SEQ ID NO:2 having at least one activity selected from the group consisting of ability to glycosylate, to bind a simple sugar or to attach to a membrane. The Examiner appears to consider the activities to be too broad and not commensurate with the enablement provided by the disclosure with regard to the allegedly extremely large number of polynucleotides encompassed by the claims. The Examiner contends that there is need for teaching exactly which amino acids can be changed to modify the sequence and still retain these uses. Applicants respectfully traverse this rejection.

First, Applicants note that claim 30 is dependent on allowed claim 27. Therefore, Applicants request withdrawal of the rejection with respect to claim 30.

Applicants have amended claim 1 to delete some of the variants, such as the variants on the polynucleotide sequence and the fragments comprising the glycosyltransferase domain alone (which embodiment was folded into the embodiment reciting at least 285 contiguous amino acids of SEQ ID NO:2), have increased the polypeptide identity embodiment to 95% and have modified the language of the fragment recitation. Applicants also amended claim 12 consistent with claim 1 and have canceled claim 29. Applicants have amended claim 28 to retain the only the embodiment reciting the percent polypeptide identity, and have increased that identity to 98%. Support for this amendment can be found in the specification at, for example, paragraph [00138]. Applicants also have amended claims 1, 12 and 28 to recite the activity of the polypeptide as "a glycosyltransferase activity," acknowledged by the Examiner to be a specific activity. Support for this amendment can be found in the specification at, for example, paragraph [0078] and further defined, for example, in paragraph [0036].

In this rejection, the Examiner was not persuaded by Applicants' arguments regarding the enablement of the claims in the form submitted with the previous response. Applicants herein revisit those arguments and the current rejection with regard to the amended claims. The amended scope of claim 1 requires enablement for nucleotide sequences which vary as defined three ways: a) that they encode a polypeptide with at least 95% identity to SEQ ID NO:2; b) that they encode a fragment of 285 contiguous amino acid residues of SEQ ID NO:2 comprising the glycosyltransferase domain; and c) that they hybridize under very highly stringent conditions to SEQ ID NOs:1 or 3. The Examiner agrees with the Applicants that there is a high level of skill in the art for the routine methods of mutagenesis which provides a reasonable expectation of success for obtaining a desired activity of any encoded protein. As the Examiner further contends that the result of modifications is unpredictable, the Examiner seeks guidance from the specification for providing predictability for the scope of the amended claims. Applicants point out that a further requirement of these variant nucleic acid molecules is that they must encode a polypeptide with glycosyltransferase activity, as recognized by the Examiner to be specific. Therefore, one skilled in the art can use the predictable routine methods of mutagenesis to obtain a nucleic acid which encodes a polypeptide having the predictable glycosyltransferase activity and having a well-established use as a glycosyltransferase.

In regard to the regions of the nucleic acid to modify, Applicants point to the parts of the specification which describe the structural features of SEQ ID NO:2 which provide the glycosyltransferase activity, namely the glycosyltransferase domain described in paragraph [0039]. In paragraph [0076], Applicants state that amino acid residues in the glycosyltransferase domain are unamenable to alteration if the biological activity is to be preserved. Therefore, the polypeptide encoded by the polynucleotide variants encompassed by the scope of the claims likely would have no (as in the

case of 1b)) or few conservative modifications in the glycosyltransferase domain (amino acids 139 to 322 of SEQ ID NO:2). In particular, for 1a), when variants in that region are ruled out, the 29 amino acid residues out of the 581 amino acid polypeptide allowed to be modified for the 95% identical variant of claim 1a) (i.e. at least 552 out of 581 amino acid residues are identical with SEQ ID NO:2) or the 11 amino acid residues allowed to be modified for the 98% identical variant of claim 28 (i.e. at least 570 out of 581 amino acid residues are identical with SEQ ID NO:2) would likely occur in residues 1 to 138 or 323 to 581. And the specification explains, in paragraph [0077], which residues can conservatively substitute the residues in SEQ ID NO:2 to result in a polypeptide which likely would retain activity. In particular, for 1b), the at least 285 amino acid fragment would have 285 residues which encompass residues 139 to 322 (so the fragment could have residues within 37 to 138 or 323 to 424 in the 285 contiguous amino acid window in addition to residues 139 to 322 of SEQ ID NO:2, up to the full length of SEQ ID NO:2). In particular, for 1c), the skill in the art, together with the teachings of paragraph [0072] provide enablement for varying the nucleic acid and retaining hybridization under very high stringency conditions. Furthermore, supplemental information provided in the specification about the structure of a 33945 polypeptide, as represented in unmodified, full length form as SEQ ID NO:2, for example paragraphs [0022] to [0033] and [0041] to [0052], tell one of skill in the art characteristic features of a 33945 polypeptide in addition to the glycosyltransferase domain. These are defined features exhibiting conserved characteristics of known structural motifs, for example a ricin domain, a transmembrane domain and a leucine zipper, among others. Again, as noted in paragraph [0077], residues which are conserved are unamenable to alteration. While possibly able to accept more modifications than the recited glycosyltransferase domain, one skilled in the art would understand that the other conserved structural features could be modified only with caution. That understanding provides even further guidance to the rational and predictable scheme of modifications of SEQ ID NO:2 to destroy or retain 33945 activity.

Applicants further submit, as Exhibit A., Bowie et al., wherein authors conclude that "proteins are surprisingly tolerant of amino acid substitutions" (page 1306, col.2, lines 12-13). In these studies, authors performed approximately 1500 single amino acid substitution at 142 positions of the *lac* repressor and found that "about one-half of all the substitutions were phenotypically silent." Therefore, one can expect that a significant percentage of random substitutions in a given protein will result in mutated proteins with full or nearly full activity. When one makes less than random substitutions following the guidance of the Applicants in the specification (as discussed above, e.g. avoiding changes to the glycosyltransferase domain or to conserved amino acid residues and performing conservative substitutions), the expectations of retaining function are greatly increased. These are far better odds than those at issue in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), in which the court found that screening many hybridomas to find the few which fell within the claims was not undue experimentation. The question is not whether it is possible to

abolish activity of a given protein by introducing a point mutation, but rather whether one of ordinary skill can produce, without undue experimentation, mutants in which the activity is not abolished. The teachings of Bowie et al. suggest that even if one of skill in the art did not have all the guidance of the specification and the rational and predictable scheme discussed above for modifying nucleic acids of the invention wherein the encoded polypeptides have the claimed glycosyltransferase activity, there would be reasonable expectation of success for making nucleic acid molecules commensurate in scope with these claims without undue experimentation.

Applicants respectfully submit that the claims do not encompass essentially infinite possible choices of nucleic acid molecules, as they have a very narrow range of variation in their current amended form. This narrow range of variation encompassed by the claims and how to achieve that variation is enabled by the teachings of the specification, the level of skill in the art, the general tolerance of polypeptides to variation and the defined, enabled glycosyltransferase activity required by the polypeptides encoded by the variant nucleic acids. In view of these amendments and remarks, Applicants respectfully request that this rejection be withdrawn.

CONCLUSIONS

Applicants gratefully acknowledge the Examiner's indication that claim 27 is allowable and requests that claim 30, dependent on claim 27, also be judged allowable.

The Examiner also indicated that claim 2 is objected to as being dependent on a rejected base claim, but would be allowable if rewritten in independent form. In response, Applicants have rewritten claim 2 in independent form and have added new claims 31-33 to be dependent on claim 2. Applicants respectfully request allowance of claims 2 and 31-33 in view of the amendment to claim 2.

Applicants respectfully request that the Examiner enter these amendments and consider these remarks after final rejection because, in view of these amendments and remarks, Applicants respectfully submit that the rejections and objections of claims 1 and claims 2-7, 12, 18, 25-26, 28 and 30 under 35 U.S.C. § 112 are herein overcome and that this application is now in condition for allowance. Early notice to this effect is solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the allowance of the subject application, the Examiner is encouraged to call the undersigned. If the Examiner disapproves of Applicants' amendments and/or remarks in this response, Applicants request a prompt mailing of an Advisory Action to that effect.

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This paper is being filed timely within two months of the mailing date of the final action. No extensions of time are required. In the event any extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the amendments and remarks made herein is respectfully requested.

Respectfully submitted,

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